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COAGULATION ACTIVITY AND D-DIMER IN SEPSIS PATIENTS

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ABSTRACT

Sepsis is a systemic inflammatory response with the presence of suspected or proven infection. The inflammation will increase the production of proinflammatory cytokines that will activate coagulation and suppress fibrinolytic system. An imbalance of hemostasis mechanism and inflammation in sepsis can progress into Disseminated Intravascular Coagulation (DIC). The objective of this study was to determine the coagulation activity (platelet count, Prothrombin Time (PT), activated Partial Thromboplastin Time (aPTT)), and D-dimer in sepsis patients. A descriptive study was conducted at the Dr. M. Djamil Hospital on December 2012-July 2013. Subjects were adult patients with two or more of four criteria for Systemic Inflammatory Response Syndrome (SIRS) and presence of suspected or proven infection admitted to the Department of Internal Medicine. Laboratory examination was conducted in the Clinical Pathology Laboratory Dr. M. Djamil Hospital including the coagulation activity and D-dimer level. Data were processed manually and presented in distribution tables, and diagrams. Subjects of this study were 54 sepsis patients, consisting of 57% males and 43% females with a median age of 53.5 year-old, platelet count 188.5 x 103/µL, PT 13.7 seconds, aPTT 39.3 seconds, and D-dimer level 1.15 µg/mL. Based on this research it can be concluded that coagulation activity in sepsis patients showed that platelets count were still in the normal range while PT and aPTT were prolonged and D-dimer levels were increased.

Key words: Coagulation activity, D-dimer, sepsis

INTRODUCTION

The American College of Chest Physicians (ACCP) and The Society for Critical Care Medicine (SCCM) define sepsis as an inflammatory reaction with symptoms of systemic inflammatory response with the presence of suspected or proven infection.[1] Sepsis is a continuous process that started from infection, SIRS, sepsis, severe sepsis, septic shock and multiorgan dysfunction that can lead to death.[2]

The incidence of sepsis reached 750,000 cases a year and more than 28.6% or about 210,000 died.[3] The most common complication of sepsis is multiple organ failures, which consists of liver dysfunction in 20%-50% of sepsis patients with DIC and 25% -67% of sepsis cases with renal dysfunction.[4] Engel *et al.* reported that severe sepsis could cause death by 63% due to renal dysfunction.[5]

Normal body responses to fight infections in sepsis is by releasing a wide variety of pro-inflammatory mediators that can stimulate activation of coagulation system in sepsis initially stimulated by the tissue factor pathway (extrinsic pathway), mediated by several pro-inflammatory cytokines. Extrinsic pathway the dominant mechanism that activates the coagulation system in sepsis will eventually increase production of thrombin.[6] Contact factors in the intrinsic pathway are also activated due to endothelial damage caused by bacteria and its substances that increases fibrin formation. The cascade of coagulation in sepsis causes an imbalance of hemostasis mechanism accompanied by inflammation that can progress to Disseminated Intravascular Coagulation (DIC).[6,7] The coagulation activity can be assessed by examination of the platelet count, PT, and aPTT. Fibrinolysis function decreases in sepsis despite persisting coagulation activity, causing greatly increased fibrin formation and eventually microvascular thrombosis. Fibrinolysis activity can be assessed by D-dimer measurement.[8,9]

There are no studies about coagulation activities and D-dimer in sepsis patients at the Dr. M. Djamil Hospital, Padang. The aimed of this study was to determine the coagulation activity (platelet count, PT, aPTT) and D-dimer in sepsis patients.

METHODS

A descriptive study was conducted at the Dr. M. Djamil Hospital during December 2012-July 2013. Subjects of this study were patients who met the inclusion and exclusion criteria. The inclusion criteria were adult patients with two or more of four criteria for SIRS and presence of suspected or proven infection who were willing to participate in this study by signing an informed consent. Exclusion criteria were patients that received anticoagulant therapy, with liver and kidney dysfunction. Samples were seven mL blood obtained by venous puncture consisting of three mL EDTA blood for platelet count, two mL citrated blood for PT-APTT examination, and two mL heparinized blood for D-dimer examination. The method of PT-aPTT examination was by electromechanical clot detection and the method of D-Dimer examination by ELISA method. The data were processed manually, and presented in distribution tables and diagrams.

RESULTS AND DISCUSSION

This research was conducted on 54 sepsis patients who were admitted to the Department of Internal Medicine, Dr. M. Djamil Hospital, Padang from December 2012 to July 2013. Data on age, gender, the activity of coagulation parameters and levels of D-dimer were recorded for all patients. This study comprised sepsis patients characteristics by age, sex and the median age of patients with sepsis was 53.5 years, the highest percentage suffered by the elderly group 70.4% and in adult group 29.6%. Distribution of sepsis patients was based on gender, 57% males and 43% females (Table 1).

Table 1. Characteristic of 54 sepsis patients

Total patients (person)	54
Age (median; range)	53.5 years old (21-74)
18-59 years old (adult)	29.6%
>60 years old (elderly)	70.4%
Sex	
Males	57%
Females	43%

Sepsis patients had normal platelet counts 59% (32/54) and with thrombocytopenia 41% (22/54) (Table 2).

Table 2. Frequency distribution of platelet counts in sepsis patients

No	Thrombocyte counts	Frequences	%
1	Normthrombocytes	32	59
2.	Low thrombocytes	22	41

Sepsis patients with shortened PT, normal PT, and elevated PT were 5.6%, 42.6%, and 51.8% (Table 3). Sepsis patients with shortened aPTT, normal aPPT, and elongated aPPT were 11%, 33.4%, and 55.6% (Table 4).

Table 3. Frequency distribution of PT in sepsis patients

PT (Sec)	Frequences	%
<9.9	3	5.6
9.9-13.5	23	42.6
>13.5	28	51.8
Total	54	100

Table 4. Frequency distribution of aPTT in sepsis patients

aPTT (Sec)	Frequences	%
<28	6	11
28-37.8	18	33.4
>37.8	30	55.6
Total	54	100

Sepsis patients with negative D-dimer (≤ 0.5 ug/mL) were 44.4% (24/54) and with positive D-dimer (>0.5 ug/mL) were 55.6% (30/54) (Figure 1).

Coagulation activity and D-dimer in 54 sepsis patients, with a median of platelet counts 188.5 x 10^3/µL, median of PT 13.7 sec, median of aPTT 39.3 sec and median of D-dimer level 1.15 ug/mL (Table 5).

Table 5. Coagulation activity and D-dimer level in 54 sepsis patients

Parameters	Median (range)
Thrombocyte counts	188.5 x 10^3 / µL (12x10^3-503x10^3)
PT	13.7 sec (9.2-96.9)
aPTT	39.3 sec (23.9-180)
D-dimer level	1.15 µg/mL (0.1-4)

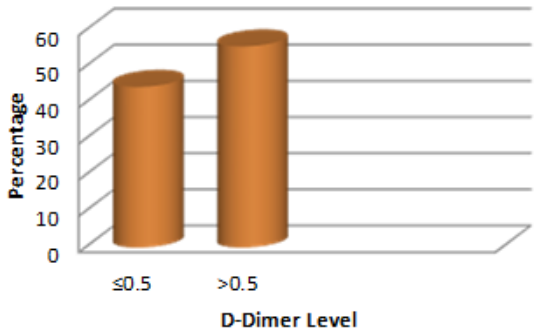

Figure 1. D-dimer level in sepsis patients

The percentage of sepsis patients that investigated based on age in this study over 60 years old (elderly) were 70.4%, with a median of age 53.5 years old (21-74 years). Oberhofer *et al.* reported that the median of age in sepsis patients was 66 years-old (22-77 years) in Kroasia.[10] This condition is associated with immune system function decreasing with age. The ability of immunity decreased in infection.[11,12] Sepsis patients in this study consisted of males 57% (30 people) and females 43% (24 people), while Park *et al.* reported sepsis patients in Korea composed of 48% males and 52% females.[13]

This study showed that the median of platelet count was in normal limits 188.5 x 10^3/µL ($12x10^3$-$503x10^3$), it was not different from a research by Lorente *et al.* in Spain, who reported a median of platelet counts in sepsis patients $192x10^3$/µL ($131x10^3$-$273x10^3$).[14] This study found thrombocytopenia in 40.7% of sepsis patients. Thrombocytopenia state is a marker of failure in bone marrow functions in maintaining hemostasis due to excessive consumption on DIC and endothelial damage because of diffuse inflammatory process.[15,16]

Median of PT was 13.7 seconds in this study (9.2-96.9 seconds) showing elongated PT in 51.8%, normal PT 42.6%, and shortened PT 56% in sepsis patients. Kinasewitz *et al.*, in the United States also obtained elongated PT with a median of 18.7 seconds (16.5-22 seconds).[17] Estrin *et at.*, in the United States researched on sepsis-DIC animals, with a median of PT 12.8 seconds.[18]

This study showed a median of APTT 39.3 seconds (23.9-180 seconds), elongated aPTT 55.6%, normal aPTT 33.4%, and shortened aPTT 11%. Lorente *et al.* reported a median value of aPTT in sepsis patients in the normal limit of 32 seconds.[14]

Fibrinolysis activity assessed by examination of D-dimer levels, increased with a median 1.15 µg/mL (0.1 to 4 µg/mL), it was same as Kinasewitz's study in 2004, who found a median of D-dimer 4.2 ug/mL (2.2-8.4 µg/mL).[17] Mayrommatis *et al.* reported 40 of 82 patients with sepsis had positive D-dimer levels (>0.5 µg/mL).[19] This study showed that D-dimer levels were positive in 30 sepsis patients (55.6%).

Thrombocytopenia, prolongation of PT and aPTT, increased levels of D-dimer in sepsis is a description of hemostasis function disorder due to the occurrence of DIC and as a parameter for detecting sepsis complications.[16] These results were associated with the occurrence of a hypercoagulable state due to activation of coagulation, caused by proinflammatory cytokines that were increased in early sepsis. Normal liver function a compensated situation leading to the value of PT and aPTT shortened or normal in sepsis.[15]

CONCLUSION AND SUGGESTION

The normal range of platelet counts, prolonged PT and aPTT, and positive D-dimer levels are coagulation activities that can be found in sepsis patients. There is a widespread agreement that dysfunctions in coagulation develop during sepsis and lead to inappropriate intravascular fibrin deposition. Any consensus beyond that statement, however, remains frustratingly elusive. In patients with severe sepsis and Disseminated Intravascular Coagulation (DIC), the parameters should be determined for detecting complications sepsis such as fibrinogen levels in order to diagnose DIC, and some of the proinflammatory cytokines that increased in early sepsis.

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